US009511085B2

(12) **United States Patent**
Kim et al.

(10) **Patent No.: US 9,511,085 B2**
(45) **Date of Patent: Dec. 6, 2016**

(54) **METHOD FOR CONTROLLING CANCER METASTASIS OR CANCER CELL MIGRATION BY MODULATING THE CELLULAR LEVEL OF LYSYL TRNA SYNTHETASE**

(75) Inventors: **Sunghoon Kim**, Seoul (KR); **Jin Woo Choi**, Seoul (KR)

(73) Assignee: **Medicinal Bioconvergence Research Center**, Suwon (KR)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 897 days.

(21) Appl. No.: **13/059,006**

(22) PCT Filed: **Aug. 18, 2008**

(86) PCT No.: **PCT/KR2008/004785**

§ 371 (c)(1),
(2), (4) Date: **Mar. 24, 2011**

(87) PCT Pub. No.: **WO2010/021415**

PCT Pub. Date: **Feb. 25, 2010**

(65) **Prior Publication Data**

US 2011/0189195 A1 Aug. 4, 2011

(51) **Int. Cl.**

C07K 16/30	(2006.01)
C12N 15/113	(2010.01)
A61K 38/17	(2006.01)
A61K 39/395	(2006.01)
A61K 31/7088	(2006.01)
C12N 9/00	(2006.01)
G01N 33/50	(2006.01)
A61K 48/00	(2006.01)

(52) **U.S. Cl.**

CPC ***A61K 31/7088*** (2013.01); ***C12N 9/93*** (2013.01); ***C12N 15/1137*** (2013.01); ***C12Y 601/01006*** (2013.01); ***G01N 33/5017*** (2013.01); *A61K 48/00* (2013.01); *C12N 2310/11* (2013.01); *C12N 2310/14* (2013.01)

(58) **Field of Classification Search**

CPC C07K 16/30; A61K 39/395; A61K 39/39558; A61K 38/17

USPC 424/155.1, 152.1; 530/389.7, 350

See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

2008/0219981 A1* 9/2008 Shimada et al. 424/138.1

OTHER PUBLICATIONS

Kim et al. (FASEB J., 2012, 26, 4142-4159).*

Narumi et al. (Jpn. J. Cancer Res. 90, 425-431, Apr. 1999).*

I. Carmi-Levy et al., "Diadenosine tetraphosphate hydrolase is part of the transcriptional regulation network in immunologically activated mast cells", Molecular and Cellular Biology, vol. 28(18), pp. 5777-5784 (Jul. 21, 2008).

S. Gyu Park et al., "Aminoacyl tRNA synthetases and their connections to disease", Proceedings of the National Academy of Sciences, vol. 105(32), pp. 11043-11049 (Aug. 12, 2008).

S. Gyu Park et al., "Do aminoacyl-tRNA synthetases have biological functions other than in protein biosynthesis?", IUBMB Life, vol. 58(9), pp. 556-558, Sep. 2006.

S. Gyu Park et al., "Functional expression of aminoacyl-tRNA synthetases and their interacting factors: new perspectives on housekeepers", Trends in Biochemical Sciences, vol. 30(10), pp. 569-574 (Oct. 2005).

S. Gyu Park et al., "Human lysyl-tRNA synthetase is secreted to trigger proinflammatory response", Proceedings of the National Academy of Sciences, vol. 102(18), pp. 6356-6361 (May 2005).

E. Rayburn et al., "Antisense, RNAi, and gene silencing strategies for therapy: Mission possible or impossible?", Drug Discovery Today, vol. 13(11-12), pp. 513-521 (Jun. 2008).

S. Won Lee et al., "Aminoacyl-tRNA synthetase complexs: beyond translation", Jrl of Cell Science, vol. 177(17), pp. 3725-3734 (Aug. 2004).

* cited by examiner

Primary Examiner — Yan Xiao

(74) *Attorney, Agent, or Firm* — Mintz Levin Cohn Ferris Glovsky and Popeo, P.C.; Kongsik Kim; Richard B. Emmons

(57) **ABSTRACT**

The present invention relates to a novel function of lysyl tRNA synthetase (KRS) which enhances tumor cell migration and affects cancer metastasis via KRS's interaction with laminin receptor (67LR) by its translocation to membrane. More particularly, the present invention relates to a method for modulating cancer metastasis or migration, which comprises regulating intracellular levels of KRS; a composition for preventing or treating cancer; use of expression vector for inhibiting the expression of KRS; a method for preventing or treating cancer; use of an agent for inhibiting an activity of KRS; a method for screening an agent which modulates cancer metastasis or migration; and a method for screening an agent which inhibits the interaction of KRS with 67LR, by said novel function. Thus, KRS can modulate cancer metastasis or migration and furthermore, can modulate intracellular metabolism related to 67LR. The interaction between KRS and 67LR can be used effectively in treating, preventing and/or diagnosing of various diseases or disorders related to the interaction.

4 Claims, 17 Drawing Sheets